Resolution of Left Atrial Appendage Thrombus with Apixaban in a Patient with Heart Failure

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Abstract:
The effect of non-vitamin K antagonist oral anticoagulants on left atrial appendage (LAA) thrombus has not been fully elucidated. There are a few reports showing resolution of LAA thrombus with apixaban. An 84-year-old woman was admitted to our hospital due to acute exacerbation of chronic heart failure and marked tachycardia with atrial fibrillation. She had permanent atrial fibrillation and was treated with warfarin; however, transthoracic echocardiography revealed a non-mobile thrombus in the LAA. Therefore, we switched warfarin to apixaban at a dose of 5 mg/day. After two weeks on that therapy, the thrombus in the LAA was successfully resolved.

Key words: left atrial appendage thrombus, atrial fibrillation, heart failure, apixaban

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Introduction

In patients with heart failure (HF) with a reduced left ventricular (LV) ejection fraction, the presence of atrial fibrillation (AF) carries a two-fold increased risk of ischemic stroke compared to normal sinus rhythm (1). AF predisposes patients to the development of atrial thrombi, most commonly in the left atrial appendage (LAA), which is the dominant source of embolism (>90%) in nonvalvular AF (2). Warfarin is used to prevent thrombotic complications with AF patients and the resolution of LAA thrombus (3). Apixaban is superior to warfarin in the prevention of thromboembolic complications in patients with AF (4), and a few case reports have described the resolution of LAA thrombus with apixaban (5, 6). However, whether or not apixaban is effective for the treatment of LAA thrombus remains unclear. We herein report a case of heart failure complicated by LAA thrombus that was successfully resolved with apixaban.

Case Report

An 84-year-old woman was admitted to our hospital with acute exacerbation of chronic heart failure. On hospital admission, she presented with functional New York Heart Association class IV. Her medical history included hypertension, chronic heart failure, permanent atrial fibrillation, and hyperthyroidism. Given her high thromboembolic risk (CHA2DS2VASc score = 5), she had been pretreated with warfarin at a dose of 1 mg/day by her practitioner. In the 3 months prior to hospitalization, her prothrombin time international normalized ration (PT-INR) values had ranged from 1.11 to 1.15, and her warfarin treatment time in the therapeutic range was 0%.

A physical examination showed coarse crackles over both lungs, an irregular heartbeat, and a grade II/VI systolic murmur at the apex. Chest X-ray revealed cardiomegaly and pulmonary congestion (Fig. 1A). Electrocardiogram showed atrial fibrillation with a ventricular heart rate of 127. Blood tests revealed plasma B-type natriuretic peptide (BNP), 2,000 pg/mL; D-dimer, 3.3 μg/mL; and PT-INR, 1.20. Since the PT-INR was not well controlled at the time of hospital admission, we switched the patient’s warfarin to apixaban at 5 mg/day.

Due to her rapid heart rate and congestive heart failure, diuretics and β-blockers were administered, and pimobendan was added. Transthoracic echocardiography (TTE) revealed left ventricular dysfunction with an LV ejection fraction of 31% and left atrial enlargement with an LA diameter of...
Color flow Doppler echocardiography showed moderate mitral regurgitation (MR) without any findings of rheumatic heart disease, prolapse, or endocarditis. The MR was likely due to LV dilatation (functional MR). TTE also showed a small thrombus (13.9×11.8 mm) in the LAA (Fig. 2A). Myocardial perfusion scintigraphy showed no evidence of ischemia or old myocardial infarction.

TTE three days later showed no remarkable changes in the thrombus in the LAA (Fig. 2B). After 9 days of apixaban treatment, TTE showed a decrease in the thrombus size (6.2×4.3 mm) (Fig. 2C). After 2 weeks, we could not detect the thrombus in the LAA by TTE. (Fig. 2D). After 4 days of apixaban treatment, her D-dimer level decreased (1.5 μg/mL) with neither prolongation of PT-INR nor activated partial thromboplastin time.

Her symptoms were ultimately relieved, and the plasma BNP level improved to 744.8 pg/mL on day 14. Chest X-ray on day 19 revealed improvement of the pleural effusion and CT of the chest. X-ray images of the chest obtained on admission (A) and on day 19 (B).

**Figure 2.** The clinical course of the left atrial appendage (LAA) thrombus demonstrated by trans-thoracic echocardiography (TTE). TTE obtained on the day after admission showing a non-mobile thrombus (13.9×11.8 mm) in the LAA (A). Subsequent TTE showed no remarkable change in the thrombus on day 3 after admission (B) but a decrease to 6.2×4.3 mm on day 9 after admission (C) and disappearance after 2 weeks of anticoagulant therapy with apixaban (D). The arrows show the thrombus in the LAA.
and increased bleeding risk (12). In the present case, we se-

in patients receiving warfarin may be predisposed to a reduced efficacy for a reduced time in the therapeutic range, and patients re-\n
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diabetes, systemic embolisms, or strokes.

Discussion

A reduced LV ejection fraction is independently associated with stroke (7), and the combination of HF with a re-
duced ejection fraction with AF doubles the risk of stroke compared to AF alone (8). The efficacy of long-term war-
farin therapy for the prevention of stroke in patients with AF

is well-established (9). However, non-vitamin K antagonist
oral anticoagulants (NOACs) have been established as safe and effective first-line medications for the prophylaxis of
thromboembolism in patients with AF (10). Approximately
35% of Apixaban for Reduction in Stroke and Other Throm-
boembolic Events in Atrial Fibrillation (ARISTOTLE) pa-
tients had heart failure, defined as an LV ejection fraction ≤
40% or symptomatic heart failure within the previous 3
months (11). That study showed that apixaban at 5 mg twice daily was superior to warfarin in preventing stroke and sym-
temic embolism and was associated with significantly lower rates of major bleeding (11). HF is a recognized risk factor for a reduced time in the therapeutic range, and patients re-
ceiving warfarin may be predisposed to a reduced efficacy and increased bleeding risk (12). In the present case, we se-
p ected apixaban due to the patient’s old age and low body

Weight.

TTE showed a thrombus in the LAA during warfarin ad-
ministration. Watanabe et al. reported that LA blood stasis resulting from heart failure led to thrombus formation even under anticoagulant therapy with warfarin (13). In addition, a previous study reported that HF was an independent nega-
tive predictor of LA thrombus resolution in patients with AF
receiving oral anticoagulation (14).

In our patient, successful thrombus resolution was ob-
tained after 2 weeks on a reduced dose of apixaban at 2.5
mg twice daily. Warfarin therapy in patients with intracar-
diac thrombus is effective in reducing the size of a thrombus by inducing a relative predominance of plasma fibrinolytic activity over anticoagulation-inhibited thrombin activity (15). However, the effect of NOACs on intracardiac thrombus has not been fully elucidated, and whether or not apixaban ther-

apy is effective in decreasing the size of an intracardiac thrombus is unclear. There have been a few case reports showing the resolution of LA thrombus after apixaban ad-
ministration (5, 6), which is likely an effect of apixaban shifting the coagulation/fibrinolysis balance to a relative pre-
dominance of fibrinolytic activity. In the present case, the D-dimer levels decreased with the resolution of the LA thrombus, with neither prolongation of the PT-INR nor the activated partial thromboplastin time.

However, another case report described the occurrence of embolic stroke during apixaban therapy for LAA throm-
bus (16). It is therefore necessary to monitor patients for
thromboembolic complications after the initiation of apix-
aban for treating pre-existing LAA thrombus. Future studies in a large population should investigate the utility of apix-
aban and other NOACs in resolving LAA thrombus.

The authors state that they have no Conflict of Interest (COI).

References

4. Ruff CT, Giugliano RP, Braunwald E, et al. Comparison of the ef-
ficacy and safety of new oral anticoagulants with warfarin in pa-
6. Dobashi S, Fujino T, Ikeda T. Use of apixaban for an elderly pa-
7. Hays AG, Sacco RL, Rundek T, et al. Left ventricular systolic dysfunction and the risk of ischemic stroke in a multiethnic popu-


